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Declaration under Rule 4.17:

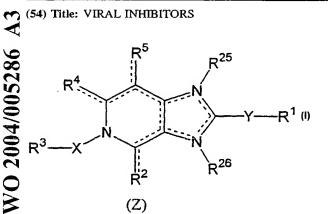
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: VIRAL INHIBITORS



(57) Abstract: The present invention relates to a pharmaceutical composition for the treatment or prevention of viral infections comprising as an active principle at least one imidazo[4,5-c]pyridine derivative having the general formula (Z): (formula). The invention also relates to processes for the preparation of compounds according to the invention having above mentioned general formula and their use as a medicine or to treat or prevent viral infections.

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CLASSIFICATION OF SUBJECT MATTER PC 7 CO7D471/04 A61K //(C07D471/04,235:00, A61K31/437 A61P31/12 221:00) According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07D A61K A61P Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Category ' Citation of document, with indication, where appropriate, of the relevant passages GB 2 158 440 A (ERBA FARMITALIA) 1 Α 13 November 1985 (1985-11-13) page 4, line 3 -page 7; claims 1,9 DATABASE CAPLUS 'Online! 1 Α CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; YUTILOV, YU. M. ET AL: "Synthesis and antiviral activity of spinaceamine" retrieved from STN Database accession no. 110:165603 XP002265211 abstract & KHIMIKO-FARMATSEVTICHESKII ZHURNAL, vol. 23, no. 1, 1989, pages 56-9, -/--Patent family members are listed in annex. Further documents are fisted in the continuation of box C. Special categories of cited documents: *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention 'E' earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is clied to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-'O' document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. other means document published prior to the international filing date but later than the priority date claimed *&* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 05/01/2004 16 December 2003 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentlaan 2

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Internat Application No
PCT/RE 03/00117

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PCT/BE 03/00117
Category •	Citation of document, with indication, where appropriate, of the relevant passages	Delawat to claim At-
	passages	Relevant to claim No.
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; HORVATH, A. ET AL.: "Preparation of sunstituted nitrogen-containing heterocyclic compounds" retrieved from STN Database accession no. 132:222537 XP002265212 RN=261379-92-4 & HU 78 019 A (HORVATH) 28 May 1999 (1999-05-28)	7
X	WO 99 27929 A (MERCK) 10 June 1999 (1999-06-10) example 4 (6)	7
x	WO 96 11192 A (SEARLE) 18 April 1996 (1996-04-18) page 207, example 358c	7
x	WO 96 12703 A (SEARLE) 2 May 1996 (1996-05-02) examples 11,18	7
x	US 5 302 601 A (KHANNAL ISH K ET AL) 12 April 1994 (1994-04-12) examples	7
X	EP 0 344 414 A (SEARLE & CO) 6 December 1989 (1989-12-06) examples	7
(WO 95 16687 A (ABBOTT LAB) 22 June 1995 (1995-06-22) examples	.7
P, X	HISASHI AKAMATSU ET AL.: "New efficient route for solid-phase synthesis of benzimidazole derivatives" JOURNAL OF COMBINATORIAL CHEMISTRY., vol. 4, no. 5, 2002, pages 475-483, XP002265210 AMERICAN CHEMICAL SOCIETY, WASHINGTON., US ISSN: 1520-4766 pages 479, 480, compounds 15,16(21),	7
	16(22)	

onal application No. PCT/BE 03/00117

Box i	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1.	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
2. X	Claims Nos.: 7-14 (in part) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
з. [Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)
This inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the Invention first mentioned in the claims; it is covered by claims Nos.:
Remark	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 7-14 (in part)

Present claims 7-14 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formula I described in page 19, line 15 - page 22, line 9.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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	· · · · · · · · · · · · · · · · · · ·		·		GCT\RF	03/00117
	atent document d in search report		Publication date		Patent family member(s)	Publication date
GB	2158440	Α	13-11-1985	BE	902611 A1	30-09-1985
				DE	3521303 A1	31-10-1985
_				JP	61167687 A	29-07-1986
HU	78019	Α	28-05-1999	НИ	78019 A2	28-05-1999
WO	9927929	Α	10-06-1999	US	6015817 A	18-01-2000
				AU	1611099 A	16-06-1999
				CA	2311923 A1	10-06-1999
				ĒΡ	1035850 A1	20-09-2000
				WO	9927929 A1	10-06-1999
MU	9611192	A	19 04 1006		5505400.4	
MU	2011126	n	18-04-1996	US	5585492 A	17-12-1996
				AT	224381 T	15-10-2002
			•	AU	3686595 A	02-05-1996
				CA	2202371 A1	18-04-1996
			•	DE	69528287 D1	24-10-2002
				DE	69528287 T2	31-07-2003
				DK	804427 T3	27-01-2003
				EP	1221441 A2	10-07-2002
				EP	0804427 A1	05-11-1997
	. *			ES	2183886 T3	01-04-2003
				JP	10512848 T	08-12-1998
				PT	804427 T	31-01-2003
			•	WO	9611192 A1	18-04-1996
				US	5719306 A	17-02-1998
WO	9612703	- A	02-05-1996	US	5635514 A	03-06-1997
				AU	3684795 A	15-05-1996
			•	WO	9612703 A1	02-05-1996
				ÜS	5688822 A	18-11-1997
US	5302601	 А	12-04-1994	US	4914108 A	02-04 1000
		• •	22 01 1554	US	5019581 A	03-04-1990 28-05-1991
				US	5227384 A	
				AT	112774 T	13-07-1993
				ΑÚ	3127089 A	15-10-1994
				CA	1337072 C	14-09-1989
				DE	68918755 D1	19-09-1995
				DE	68918755 T2	17-11-1994
				DK	121189 A	09-03-1995
				EP	0344414 A1	15-09-1989
						06-12-1989
				ES FI	2061753 T3	16-12-1994
					891200 A ,B,	15-09-1989
				JP	1316378 A	21-12-1989
	•			JP	2714426 B2	16-02-1998
				NO	891058 A ,B,	15-09-1989
				NZ	228336 A	29-01-1992
				PH	26967 A	28-12-1992
			•	ZA	8901926 A	30-05-1990
				PT	90208 A	10-11-1989
	0344414	Α	06-12-1989	US	4914108 A	03-04-1990
EP (US	5019581 A	28-05-1991
EP (
EP (AT	112774 T	15-10-1994
EP (AT AU	112774 T 3127089 A	15-10-1994 14-09-1989
EP (15-10-1994 14-09-1989 19-09-1995

Intermation on patent family members

Interna Application No
PCT/BE 03/00117

<u> </u>		101/ DE 03/ 0011/			
Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 0344414	Α		DE	68918755 T2	09-03-1995
			DK	121189 A	15-09-1989
			EP	0344414 A1	06-12-1989
			ES	2061753 T3	16-12-1994
			FI	891200 A ,B,	15-09-1989
			JP	1316378 A	21-12-1989
			JP	2714426 B2	16-02-1998
			NO	891058 A ,B,	15-09-1989
			NZ	228336 A	29-01-1992
			PH	26967 A	28-12-1992
			US	5227384 A	13-07-1993
			US	5302601 A	12-04-1994
			ZA	8901926 A	30-05-1990
			PT	90208 A	10-11-1989
WO 9516687	Α	22-06-1995	US	5486525 A	23-01-1996
			ΑT	212992 T	15-02-2002
			ΑU	690620 B2	30-04-1998
			ΑU	1303695 A	03-07-1995
			BR	1100809 A3	23-11-1999
			CA	2176247 A1	22-06-1995
			DE	69429827 D1	21-03-2002
			DE	69429827 T2	21-11-2002
			DK	734386 T3	27-05-2002
			EP	0734386 A1	02-10-1996
			ES	2173171 T3	16-10-2002
			JP	9507474 T	29-07-1997
			PT	734386 T	31-07-2002
			WO	9516687 A1	22-06-1995